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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/265,540	03/08/99	PARHAM C	DX0304K

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HM22/1022

EXAMINER	
WEGERT, S	
ART UNIT	**PAPER NUMBER**
1647	12

DATE MAILED: 10/22/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/265,540	Applicant(s) PARHAM ET AL.	
	Examiner Sandra Wegert	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-11, 19, 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement received 31 August 1999 (Paper 4), and the Information Disclosure Statement received 28 December 1999 (Paper 5) have been entered into the record. Applicant's election with traverse of Invention III, (claims 12-18) in Paper No. 8 is acknowledged. Claims 1-11, 19 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

The traversal is on the ground(s) that the polypeptide of Invention I and the antibody of Inventive Group IX should be prosecuted in the same Inventive Group as that containing the polynucleotide and expression system. Applicant's arguments are not persuasive, however since the Inventions were properly restricted as separate compositions having characteristic differences in structure and function and each has an independent utility which cannot be exchanged. Furthermore, Inventive Groups I, III and IX were properly restricted as pertaining to methods that are practiced with different materials for different purposes as detailed in Paper 6 (4/27/00). Furthermore, since a complete search of the art includes a search of the art that renders an invention obvious as well as anticipatory, the additional searches required for examination of Inventions I and IX *with* Invention III would be extensive, thus presenting an undue burden for the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-18 are under examination in the Instant Application.

Informalities

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "POLYNUCLEOTIDE ENCODING MONKEY DIRS1 POLYPEPTIDE."

Appropriate correction is required.

Filing History

The specification makes reference to several Patent Applications on page 70, lines 26 and 27. Their current status must be updated.

Appropriate correction is required.

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on p. 27, line 23. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only (e.g., "The NCBI Database"). See MPEP § 608.01 (p).

Appropriate correction is required.

Claims

Claim 12 is objected to because it depends from claim 1, which is not elected.

Claims 12 and 16 are objected to because they recite or encompass non-elected inventions.

Appropriate correction is required.

Abstract

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. It should consist of one paragraph of 25 lines or less and 150 words or less.

Appropriate correction is required.

Claim Rejections/Objections

Claim Rejections - 35 USC § 112, second paragraph-indefiniteness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the limitation "said" and "said nucleic acid" in the Preamble and in 12-A)-b). There is insufficient antecedent basis for these limitations in the claims.

The term "exhibits identity" in claim 12-A)-b)-iii is an undefined term which renders the claim indefinite. The term "exhibits identity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of identity, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention defined by the term.

Claim 12 is rendered indefinite because 12-A)-b)-iv equates a polynucleotide and an expression vector. Use of "comprising" language would be remedial.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph-utility.

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 12-18 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to the polynucleotides encoding DIRS1 polypeptide, a kit comprising the polynucleotide, and methods of recombinant expression of the peptide encoded by SEQ ID NO: 2. The specification teaches results from Southern hybridization experiments in which expression of DIRS1 cDNA in a substantial number of stimulated or diseased versus normal tissues is demonstrated by using cDNA inserts of tissue-specific libraries. There is a lack

of specificity according to tissue type both across many kinds of tissues and between diseased and normal tissue. In addition, tissue-specific cDNA libraries are often incomplete, or preferentially perpetuate certain clones more than others (due to GC content of the insert, for example). Thus, presence or absence in a library cannot be accepted as evidence of differential expression patterns.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polypeptide and the polynucleotides and recombinant methods used to express it:

1) For the production of antibodies,

2) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide,

3) To produce a variant or chimeric nucleotide or polypeptide,

4) To search for physiological activity of the claimed polynucleotide encoding the polypeptide, or its ligands.

Each of these shall be addressed in turn:

1) For the production of antibodies. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the nucleotide encoding the polypeptide and antibodies against the polypeptide have no patentable utility.

2) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide. This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

3) To produce a variant or chimeric nucleotide or polypeptide. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) *To search for physiological activity of the claimed polynucleotide encoding the polypeptide, or its ligands.* Similarly, this asserted utility is credible and substantial. However, it is not specific. Such is performed for any peptide-ligand pair when the physiological role of each is not known. It is the definition of the type of further research that is required for either the claimed polynucleotide encoding the DIRS1 polypeptide or its ligand to have patentable utility.

Claims 12-18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, the specification does not reasonably provide enablement for use of the polypeptide or polynucleotide *variants* as recited in claims 12-A)-b)-i), 12-A)-b)-ii), 12-A)-b)-iii), 12-A)-b)-ix), 13-15, 16)-a), 16)-c), 17-b) and 18-b). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The breadth of the claims 12-A)-b)-i), 12-A)-b)-ii), 12-A)-b)-iii), 12-A)-b)-ix), 13-15, 16)-a), 16)-c), 17-b) and 18-b) is too large since the specification fails to provide any guidance on how to produce nucleotide fragments of SEQ ID NO: 1 or peptide fragments of SEQ ID NO: 2 and still retain the function of the claimed polynucleotides encoding the polypeptides. Claim 12-A)-b)-i) and claim 12-A)-b)-ii) refer to antigenic sequences of the polypeptide of SEQ ID NO: 2, without knowledge of the polypeptides that would fall within this range. In other words,

no discussion or working examples are disclosed as to what amino acids are necessary for the antigenic sequences. Claims 12-A)-b)-iii), 12-A)-b)-ix) and 16)-c) refer to polynucleotides that have only weak homology to the polynucleotide of SEQ ID NO: 1. The instant case claims polynucleotides, for example, that are identical over only 13 bases with the polynucleotide of SEQ ID NO: 1. The possible effect of changing even one amino acid in a polypeptide can be seen in U.S. Patent 5,350,836 (Kopchick, et al) in which several antagonists of a vertebrate growth hormone differ from the naturally-occurring growth hormone by a single amino acid (column 2, lines 37-48). Similarly, PTH and PTHrP are two structurally closely related proteins, which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). In addition, the predictability of the art is very low with regard to determining function of new receptors based on even a high degree of homology to other receptors; for receptors with *low* homology to other receptors, it would logically be difficult to predict function as well. Accurate inference of function from homology *must* be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. For example, Murdoch and Finn (2000) discuss families of cytokines in which members have high homologies -some differ by only a few amino acids-- yet very different ligand binding affinities and selectivities. These examples and others illustrate that it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

In summary, the specification does not provide a description of a repeatable process of producing, nor of working examples of making the polypeptides whose amino acid sequences deviate from the disclosed sequence (SEQ ID NO: 1) by as much as 96%. In addition, the

predictability of the art is low with regards to the knowledge of what effects altering the sequence of the polynucleotide(s) would have on the function of the DIRS1 polypeptide. For this reason, undue experimentation would be required to determine a structure-function relationship for each possible polypeptide or polynucleotide encompassed by the claims.

Due to the large quantity of experimentation necessary to determine an activity or property of the claimed polynucleotides such that it can be determined how to use the claimed polynucleotides and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion: Claims 12-13 are rejected for the reasons listed above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The

examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

10/15/01

ELIZABETH KEMMERER
PRIMARY EXAMINER